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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/092,237	03/06/2002	Steven T. Boyce	CUT/01	8680

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EXAMINER	
KAUSHAL, SUMESH	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 06/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/092,237	BOYCE, STEVEN T.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 April 2004* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's response filed on 04/15/04 has been acknowledged.

Claims 1-33 are pending and are examined in this office action.

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is ***703-872-9306****.*

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

Claim Rejections - 35 USC § 102

Claims 1-10, 13-29 and 31-33 stand rejected under 35 U.S.C. 102(b) as being anticipated by Boyce (Med. Biol. Eng. Comput. 36:791-800, 1998, ref of record), for the same reasons of record as set forth in the office action mailed on 10/21/03.

The invention as claimed is drawn to a skin device comprising cultured epidermal cells and dermal cells cultured on a biocompatible matrix.

Boyce teaches skin substitutes comprising cultured human keratinocytes, fibroblasts, melanocytes and collagen-GAG polymers. With regard to claims 1, 5-6, 10, 13-15, 18-19, 24, 28-29 and 31, the cited art teaches a cultured skin substitute comprising cultured dermal cells on Collagen-GAG matrix, which further provides a lamination layer for cultured keratinocytes. With regard to claims 2, 3, 16-17, 19-20, 25, the cited art further teaches that components of skin substitute include keratinocytes, fibroblasts, endothelial cells, smooth muscle cell, melanocytes, nerve cells, glands and hair follicles (page 792, col. 1, table-1, page 793 fig-1). With regard to claim 4, and 27 the cited art further teaches the use of skin substitutes for burns, scars cutaneous ulcers or congenital anomalies (page 791, col.1 para.1). With regard to claims 7 and 21-22 the cited art further teaches that cells in the skin substitute ranges from culture parenchymal

cells (autologous or allogenic) to tissue derivatives (i.e. xenogeneic collagens acellular dermal matrix) to synthetic polymers (page 792 col.2 para.1). With regard to claim 8 and 23 the cited art further teaches genetic modification of skin cells (page 797 col.2 para.2-3, page 794 fig-3). With regard to claim 9, 16-17, 26 the cited art further teaches that the skin substitute is capable of providing epidermal barrier, basement membrane, angiogenesis and pigmentation (page 794 col.1 para.1, col.2 para.1; page 795, col.2 para.1). The cited art further teaches the use of non-adherent highly porous dressing that allow both delivery and drainage of wound exude from grafts during the period of engraftment (page 795, col.2 para.1). Thus the cited art clearly anticipate the invention as claimed.

Claim Rejections - 35 USC § 103

Claims 11-12 and 30 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Boyce (Med. Biol. Eng. Comput. 36:791-800, 1998, ref of record) as applied to claims 1-10, 13-29 and 31-33 above, and further in view of Boyce (US 5,976,878, 1999, ref of record), for the same reasons of record as set forth in the office action mailed on 10/21/03.

Boyce teaches skin substitutes comprising cultured human keratinocytes, fibroblasts, melanocytes and collagen-GAG polymers. With regard to claims 1, 5-6, 10, 13-15, 18-19, 24, 28-29 and 31, the cited art teaches a cultured skin substitute comprising cultured dermal cells on Collagen-GAG matrix, which further provides a lamination layer for cultured keratinocytes. With regard to claims 2, 3, 16-17, 19-20, 25, the cited art further teaches that components of skin substitute include keratinocytes, fibroblasts, endothelial cells, smooth muscle cell, melanocytes, nerve cells, glands and hair follicles (page 792, col. 1, table-1, page 793 fig-1). With regard to claim 4, and 27 the cited art further teaches the use of skin substitutes for burns, scars cutaneous ulcers or congenital anomalies (page 791, col.1 para.1). With regard to claims 7 and 21-22 the cited art further teaches that cells in the skin substitute ranges from culture parenchymal cells (autologous or allogenic) to tissue derivatives (i.e. xenogeneic collagens acellular dermal matrix) to synthetic polymers (page 792 col.2 para.1). With regard to claim 8

and 23 the cited art further teaches genetic modification of skin cells (page 797 col.2 para.2-3, page 794 fig-3). With regard to claim 9, 16-17, 26 the cited art further teaches that the skin substitute is capable of providing epidermal barrier, basement membrane, angiogenesis and pigmentation (page 794 col.1 para.1, col.2 para.1; page 795, col.2 para.1). The cited art further teaches the use of non-adherent highly porous dressing that allow both delivery and drainage of wound exude from grafts during the period of engraftment (page 795, col.2 para.1).

Even though Boyce (1998) teaches a method of making skin substitute comprising variety of cultured cells the reference does not specifically teach a method of producing a cultured skin device in medium containing insulin in the range of 0.05 ug/ml to 500 ug/ml

With regard to claims 11-12 Boyce (US 5,976,878, 1999) teaches a method of making a composite skin on a laminated surface of dermal membrane (collagen-GAG), wherein the human keratinocytes are cultured in a media containing 0.5 ug/ml of insulin (col.14 line 64). With regard to claim 30 the cited art teaches dehydration of collagen matrix to form a cross-linked matrix before inoculation with dermal culture (col.12 line 45-61). Thus it would have been obvious to one ordinary skill in the art at the time of filing to incorporate insulin in the range of 0.05 ug/ml to about 500 ug/ml in the culture conditions as taught by Boyce (1998). One would have been motivated to incorporate insulin in culture media because insulin is a growth factor that increases cellular growth and proliferation. It would have been further obvious to use dehydrated laminated collagen as taught by Boyce (1998). One would have been motivated to make dried cross-lined matrix because such a preparation can be stored in a dry state for future use. Thus the invention as claimed is prima facie obvious in view of cited prior art of record.

Response to Dr. Boyce Declaration

The declaration filed by Dr. Boyce states that the prior art of record (Boyce, 1998) does not anticipate the invention as claimed because the Figure 1 of the cited reference discloses a biocompatible reticulated matrix that is filled uniformly and entirely

with cultured dermal cells, which is distinct from the claimed cultured skin device. The applicant argues that the invention as claimed is drawn to a skin device that contains cultured dermal cells on a biocompatible reticulated matrix and not to a matrix filled with dermal cells. In addition the applicant argues that Figure-1 of the cited art does not enable the invention as claimed.

Applicant's arguments filed 03/26/04 have been fully considered but they are not persuasive. Applicant's arguments do not comply with 37 CFR 1.111(c) because they do not clearly point out the patentable novelty which he or she thinks the claims present in view of the state of the art disclosed by the references cited or the objections made. Further, they do not show how the amendments avoid such references or objections.

The declaration argues that the matrix disclosed in the prior art is uniformly and entirely filled with cultured dermal cells, which is distinct from the invention as claimed. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e. cultured dermal cells deposited on a biocompatible reticulated matrix) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

In instant case it is only applicant's assumption that the skin construct as disclosed in the cited art of record is not enable and the Figure 1 of the cited reference discloses a biocompatible reticulated matrix that is filled uniformly and entirely with cultured dermal cells. However, applicant's argument are found NOT persuasive because the cited art clearly teaches that cultured skin substitutes consists of human keratinocytes and fibroblasts attached to collagen-glycosaminoglycan substrates which have been designed and tested in preclinical and clinical studies (see abstract, fig-1, fig-2, fig-4, fig-5). The cited art clearly teaches that after preparation of large preparations of skin cells, organization into skin substitutes increases (skin construct of figure- 1) anatomical fidelity to native skin in substitute (page 793 col.1 sec. 2.2.2). Therefore the cultures skin substitutes as disclosed in the prior art of record are fully enabled, especially when the cited art has demonstrated the successful healing of skin wounds in

animal. Furthermore, contrary to applicant's assumption the fig-1 of the cited reference clearly teaches that cultured human keratinocytes in vitro organize to form stratified squamous epithelium attached to dermal substitute composed of cultured human fibroblasts and collagen-GAG substrate. The disclosure of cited art of record is not limited to a skin device that contains a matrix is filled with dermal cells but encompasses cultured dermal cells present on a biocompatible matrix. Thus the applicant's argument that Figure 1 discloses a biocompatible reticulated matrix that is filled uniformly and entirely with cultured dermal cells (fibroblasts) is considered moot, since give the broadest reasonable interpretation the skin construct as disclosed in the cited art of record clearly anticipate the invention as claimed.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel Ph.D. can be reached on 571-272-0781. The fax phone

numbers for the organization where this application or proceeding is assigned is 703-872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

S.Kaushal
Patent examiner

JEFFREY FREDMAN
PRIMARY EXAMINER